

## REMARKS

Claims 1-20 are pending in the present application. Claims 22-32 have been cancelled by the above amendment.

Applicants thank the Examiner for the telephonic Interview conducted on September 9, 2003. The differences discussed between the art of record and the independent claims of the present application are set forth below.

Reexamination of the application and reconsideration of the rejections are respectfully requested in view of the above amendments and the following remarks, which follow the order set forth in the Office Action.

### **A. Claim rejections—35 U.S.C. § 103**

Claims 1-20 were rejected under 35 U.S.C. § 103 (a) as obvious over U.S. Patent No. 3,128,283 to Pappo. This rejection is respectfully traversed for the reasons given below.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. See, e.g., MPEP § 2143. Thus, to support a conclusion of obviousness, the prior art must suggest the desirability of making the claimed invention, i.e., provide a teaching or suggestion to one of ordinary skill in the art to have made the changes that would have produced the claimed subject matter. (*Ryco Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991)).

Pappo does not teach or suggest all of the claim limitations of any of independent claims 1, 6, 15, or 20, each of which recites a process for the production of oxandrolone. Each of claims 1, 6, 15, and 20 includes an initial step of oxidizing (claims 1, 6, and 20) or reacting (claim 15) mestanolone to form 17 $\beta$ -hydroxy-17 $\alpha$ -methyl-5 $\alpha$ -androst-1-en-3-one. In claims 1 and 20, mestanolone is oxidized using IBX. In claim 15, mestanolone is reacted with IBX.

Pappo teaches the production of oxandrolone in Example 5 (column 9, line 50-column 10, line 28) as well as in column 3, lines 22-41. However, Pappo teaches that the starting material for the production of oxandrolone is 17 $\beta$ -hydroxy-17 $\alpha$ -

methyl-5 $\alpha$ -androst-1-en-3-one, not mestanolone as recited in step (a) of each of independent claims 1, 6, 15, and 20.

Pappo does teach the use of mestanolone (i.e., 17 $\beta$ -hydroxy-17 $\alpha$ -methyl-5 $\alpha$ -androstan-3-one); however, Pappo teaches that mestanolone is used as the starting material for the production of 17 $\beta$ -hydroxy-17 $\alpha$ -methyl-3-oxa-A-homo-5 $\alpha$ -androstan-4-one, not the production of oxandrolone. See *Example 30* (column 16, line 31-column 17, line 23) as well as column 4, line 65-column 5, line 2. The first step of this process as taught by Pappo involves reacting 17 $\beta$ -hydroxy-17 $\alpha$ -methyl-5 $\alpha$ -androstan-3-one (i.e., mestanolone) with isopropenyl acetate to afford 17 $\alpha$ -methyl-5 $\alpha$ -androst-2-ene-3,17 $\beta$ -diol 3,17-diacetate. Pappo does not disclose oxidizing (or reacting) mestanolone to form 17 $\beta$ -hydroxy-17 $\alpha$ -methyl-5 $\alpha$ -androst-1-en-3-one as recited in claims 1, 6, 15, and 20, and does not disclose using IBX as recited in claims 1, 15, and 20.

Furthermore, there is no suggestion or motivation to modify Pappo to achieve the claimed invention. "Even when obviousness is based on a single prior art reference, there must be a showing of a suggestion or motivation to modify the teachings of that reference." *In re Kotzab*, 55 USPQ2d 1313, 1316-17 (Fed. Cir. 2000). No suggestion or motivation has been provided to modify Pappo to provide a process for the production of oxandrolone as recited in any of independent claims 1, 6, 15, or 20. As discussed above, mestanolone is not named or suggested as a starting material in the process taught by Pappo for making oxandrolone. Rather, 17 $\beta$ -hydroxy-17 $\alpha$ -methyl-5 $\alpha$ -androst-1-en-3-one is taught as being the starting material for producing oxandrolone. In addition, Pappo teaches that mestanolone is the starting material for producing 17 $\beta$ -hydroxy-17 $\alpha$ -methyl-3-oxa-A-homo-5 $\alpha$ -androstan-4-one, and further teaches that the first step of such a process is reacting mestanolone with isopropenyl acetate to afford 17 $\alpha$ -methyl-5 $\alpha$ -androst-2-ene-3,17 $\beta$ -diol 3,17-diacetate. There is no suggestion or motivation to modify Pappo to provide the processes recited in any of claims 1, 6, 15, or 20.

Therefore, independent claims 1, 6, 15, and 20 and the claims depending therefrom (i.e., claims 2-5, 7-14, and 16-19) are not obvious over Pappo because (1) the cited art does not teach all the limitations of any of independent claims 1, 6, 15, or 20 and (2) there is no motivation to modify Pappo to achieve the claimed method

in any of independent claims 1, 6, 15, or 20. Applicants respectfully request that the Examiner withdraw the 35 U.S.C. § 103 rejections of claims 1-20.

The Examiner stated the following on page 4 of the Office Action:

It would have been obvious to one skilled in the art to prepare oxandrolone by any method taught by the prior art as no specific method for preparation is claimed in these claims. ...

Claim 20 differs from claim 6 in mestanolone oxidation by IBX. Since it has not been establish (sic) any advantage or criticality of using IBX in first step, use of any oxidizing agent for oxidation of mestanolone would have [been] obvious at the time of invention.

Claims 1-5 and 15-17 and 19 were said to be allowable because of applicant's disclosure that this method gives good yield of oxandrolone as compared to prior art method. However, since no data has been provided, the said claims are now rejected on the same basis as all other claims for the reasons cited above.

No unexpected results are seen. No claim is allowed.

In contrast to the statement above, the present application does present yield data of the overall process, yield data for the first step of the process when IBX is used, and yield data of a known process. For example, the specification discusses the yield of oxandrolone as follows: "[t]he present invention provides a method for forming oxandrolone in high overall yields (e.g., 30-40%) and high purity (e.g., greater than 98%)" (*p.5, paragraph [0019], first sentence*) and "[t]he overall yield for the entire process is typically about 30% to about 40%" (*p. 10, paragraph [0025], last sentence*). The specification includes examples beginning on page 11 that illustrate an overall yield of oxandrolone of 33% (*see p. 13, paragraph [0031], last sentence*). The specification also states that "by using IBX as the oxidizing agent in the first step, the enone intermediate is produced in the present invention in high yields (e.g., about 70%)" (*p. 5, paragraph [0019], third sentence*). The specification points out that U.S. Patent No. 2,260,328 discloses a method of forming 17-hydroxy-17-methyl-5-androst-1-en-3-one from 17-hydroxy-17-methyl-5-androstan-3-one using bromination-dehydrobromination (*p. 2, paragraph [0004]*). The specification further states that "[m]ethods using bromination-dehydrobromination are disadvantageous due to low yields" and that "these methods typically generate the compound in a 15-

30% overall yield with the compound being contaminated in approximately 5-10% of methyl testosterone" (p. 2, paragraph [0005]).

Although the above portions of the specification are being pointed out for the Examiner's convenience, it is noted that, as discussed above, a *prima facie* case of obviousness has not been established. Therefore, no evidence of unexpected results is needed. See MPEP § 2142 ("If the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness."). In view of the above, Applicants respectfully request a notice of allowability for pending claims 1-20.

### Conclusion

For the foregoing reasons, pending claims 1-20 are considered allowable. A Notice to this effect is respectfully solicited. If any questions remain, the Examiner is invited to contact the undersigned attorney at the number given below.

Respectfully submitted,

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Date: October 20, 2003

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